REMARKS

Favorable reconsideration is respectfully requested in view of the above amendments and the following remarks. Following the amendments, claims 26, 28, 29, 31, 32, 36, 37, 39, 40, 43, 45-49, 51-56, 59-64, 69, 71 and 154-174 are pending and under consideration, with claims 46, 154, 161 and 169 being in independent format.

The specification has been amended to include the required headings. Previously withdrawn claims 1-4, 6-12, 15-19, 21, 24 and 25 have been cancelled. Claim 26 has been amended to depend upon independent claim 46. Claim 27 has been cancelled and claim 28 has been amended to include the subject matter of claim 27. Claim 29 has been amended to include the subject matter of cancelled claim 30. Claim 31 has been amended to depend from claim 46, and previously withdrawn claims 33-35 have been cancelled. Claim 36 has been amended to depend from claim 46, and previously withdrawn claim 38 has been cancelled. Claim 39 has been amended to depend from claim 46.

Independent claim 46 has been amended to recite a method including the use of a magnetic field that is a constant field or is a variable field with a frequency of 0.1 Hz to 10Hz. It is submitted that support for this amendment may be found, for example, on page 10, lines 19-21, of the specification and in originally filed claim 68. Claims 47, 48 and 53 have been amended to depend from claim 46 and to clarify the language of the claims. Claim 50 has been cancelled. Claims 56, 59, 60, 63 and 64 have been amended to clarify the claim language. Previously withdrawn claims 66 and 152 have been cancelled, and claim 68 has been cancelled following the incorporation of its subject matter into claim 46. Claim 71 has been amended to correct a minor typographical error.

Claims 154-174 have been added to the application. Independent claim 154 is drawn to a method for treating a patient suffering from a disorder involving an ion channel by repairing tissue or bone, the method comprising administering magnetisable particles to the patient wherein the magnetisable particles associate with cells of the patient, and manipulating an ion channel using a magnetic field external to the patient, wherein the magnetic field is a constant field, or is a variable field with a frequency of 0.1 Hz to 10Hz, and the cells are ligamentum cells, tenocytes, chondrocytes or stromal cells. Support for this claim may be found throughout the

specification and claims as originally filed. Independent claim 161 is drawn to a method for regenerating tissue by associating a magnetisable particle with an ion channel of a cell, and manipulating the ion channel using a magnetic field, wherein the cell is a ligamentum cell, tenocyte, chondrocyte or stromal cell. Support for claim 161 may be found, for example, at page 14, lines 15-16, of the specification as originally filed and in originally filed claim 60. Newly added independent claim 169 is drawn to methods of regenerating cartilage comprising associating a magnetisable particle with a TREK ion channel of a chondrocyte and manipulation said ion channel using a magnetic field, wherein the magnetisable particle is associated with the TREK ion channel by means of an antibody. Support for claim 169 may be found at page 14, lines 15-16, and throughout the specification and claims as originally filed. Newly added claims 155-160, 162-168 and 170-174, are dependent on claims 154, 161 and 169, respectively.

It is urged that support for all the above amendments may be found throughout the specification as originally filed and that none of the amendments constitute new matter or raise new issues for consideration.

Applicants note that, following these amendments, claims 26, 28, 29, 31, 32, 36, 37, 39, 40, 43, 45, 47-48 and 51-56 all depend, either directly or indirectly, from claim 46, and thus are properly included with the claims of Group II as outlined in the Restriction Requirement mailed March 8, 2007.

Claim Objections

The Examiner objected to claims 49 and 60 as containing minor typographical errors. Those errors have been corrected.

Claim rejections under 35 USC §112, first paragraph – Enablement & Written Description

Claims 46, 49, 50, 59-64, 68, 69 and 71 stand rejected under 35 USC §112, first paragraph as lacking both an enabling disclosure and an adequate written description. These rejections are respectfully traversed.

Following the above amendments, independent claim 46 is drawn to a method for treating a disorder by administering to a patient magnetisable cells that associate with an ion channel of a cell in the patient and manipulating the ion channel using an external magnetic field that is either

constant or is variable with a frequency of 0.1 to 10Hz, with newly added independent claim 154 being drawn to such a method wherein the cells are ligamentum cells, tenocytes, chondrocytes or stromal cells, and the method comprises repairing tissue or bone. Newly added independent claim 161 recites a method for regenerating tissue using a magnetisable particle and a magnetic field to manipulate an ion channel on a ligamentum cell, tenocyte, chondrocyte or stromal cell, while newly added independent claim 169 recites a method of regenerating cartilage using a magnetisable particle and a magnetic field to manipulate a TREK ion channel on a chondrocyte wherein the magnetisable channel is associated with the TREK ion channel by means of an antibody.

The instant specification clearly describes the use of magnetisable particles to treat a disorder and in the regeneration of a tissue, such as cartilage, by associating a magnetisable particle with an ion channel of a cell, for example by means of an antibody that binds to the cell, and applying an external magnetic field. As discussed in the specification, application of the magnetic field activates the ion channel, thereby affecting the electrical activity in the cell and/or intercellular communication. More specifically, Example 4 of the application describes studies demonstrating the ability of a magnetic field to alter calcium channel activity following attachment of antibody-labeled magnetic particles to cells transfected with TREK.

Furthermore, using the methods described in the instant specification, the inventors have succeeded in both up-regulating the gene osteopontin in stem cells *in vitro* and in growing cartilage in an animal model. As detailed in the attached Declaration of Professor Alicia El Haj, in the first study an anti-TREK antibody was employed to bind magnetic nanoparticles to the TREK channel in human mesenchymal stem cells. Subsequent application of a magnetic field led to up-regulation of osteopontin, which is known to be a key component in the production of cartilage. In a second study, human mesenchymal stem cells to which magnetic nanoparticles had been bound using an anti-TREK antibody were implanted into nude mice. Subsequent application of an external magnetic field to the mice resulted in the production of cartilage. These studies clearly demonstrate that one of skill in the art to which the invention pertains would be able to employ the presently claimed methods to activate cells, for example, of a chondrocyte lineage, and thereby repair and/or regenerate tissue, such as cartilage.

Applicants respectfully submit that one of skill in the art, on being provided with the instant specification, would indeed be able to practice the claimed invention and that the rejection of the claims under 35 USC §112, first paragraph, as lacking an enabling disclosure may thus be properly withdrawn.

Furthermore, in view of the high level of skill in the art, it is urged that one of skill in the art would have appreciated that the inventors were indeed in possession of the presently claimed invention at the time the application was filed, and that the rejection of the claims under 35 USC §112, first paragraph, as lacking an adequate written description, may be properly withdrawn.

Claim rejections under 35 USC §112, second paragraph

Claims 46, 49, 50, 59-64, 68, 69 and 71 stand rejected under 35 USC §112, second paragraph as being indefinite. Specifically, the Examiner has objected to the claims as including improper Markush groups, and for including the terms "ion channels" and "manipulating", and both "tumor cell" and "cancer cell". In addition, the Examiner has objected to claims 59-64 as being unclear.

In response, claims 59, 63 and 64 have been amended to remove the term "and/or", claim 46 has been amended to clarify that the magnetisable particles associate with an ion channel of a cell, and claims 59-64 have been amended as recommended by the Examiner to clarify how they depend from claim 46. With regards to the Examiner's objection to the term "manipulating an ion channel", it is submitted that one of skill in the art, on being provided with the instant specification, would appreciate that this term refers to changing the conformational state of the ion channel, as stated, for example, in paragraph 0031 of the published application.

Applicants respectfully submit that, following entry of the above amendments, one of skill in the art would clearly be able to determine the metes and bounds of all the pending claims, and that the rejection of the claims under 35 USC §112, second paragraph, may thus be properly withdrawn.

Claim rejections under 35 USC §102

Claim 46 stands rejected under 35 USC §102(b) as being taught by Yanase et al. (Japanese Journal of Cancer Research, 89:463-469, 1998).

Yanase et al. disclose studies in which magnetic particles were associated with glial cells and then implanted into rats. Subsequent application of a high frequency alternating magnetic field of 118 kHz killed the glioma cells without heating other parts of the rats' bodies.

In contrast, as noted above, amended independent claim 46 is drawn to methods for treating a disorder by administering to a patient magnetisable cells that associate with an ion channel of a cell in the patient and manipulating the ion channel using an external magnetic field that is either constant or is variable with a frequency of 0.1 to 10Hz. Similarly, newly added independent claim 154 is drawn to a method of repairing tissue or bone by administering at least one magnetisable particle to a patient wherein the magnetisable particle associates with a cell of the patient, and manipulating an ion channel of the cell using an external magnetic field that is a constant field or is a variable field with a frequency of 0.1 to 10 Hz. Yanase et al. do not teach or suggest the use of a magnetic field that is constant or is a variable field with a frequency of 0.1-10 HZ to manipulate an ion channel of a cell in order to treat a disorder. It is thus submitted that the subject matter of independent claims 46 and 154 is both novel and non-obvious over the teachings of Yanase et al.

Furthermore, Yanase et al. do not teach or suggest a method of regenerating tissue by associating a magnetisable particle with an ion channel of a cell and manipulating the ion channel using a magnetic field, wherein the cell is a ligamentum cell, tenocyte, chondrocyte or stromal cell, as recited in newly added independent claim 161. Nor do they teach or suggest a method for regenerating cartilage by associating a magnetisable particle with a TREK ion channel of a chondrocyte by means of an antibody, and manipulating the ion channel using a magnetic field, as recited in newly added independent claim 169.

Applicants respectfully submit that none of the presently pending claims are either anticipated or rendered obvious by the disclosure of Yanase et al., and that the rejection of the claims under 35 USC §102(b) may thus be properly withdrawn.

Concluding Remarks

An Information Disclosure Statement is submitted herewith, together with a Request for a Three Month Extension of Time, extending the deadline for responding to the Restriction Requirement to January 12, 2008.

Should the Examiner have any remaining concerns regarding the subject application, he is respectfully requested to telephone the undersigned at 206.382.1191.

Respectfully submitted,

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